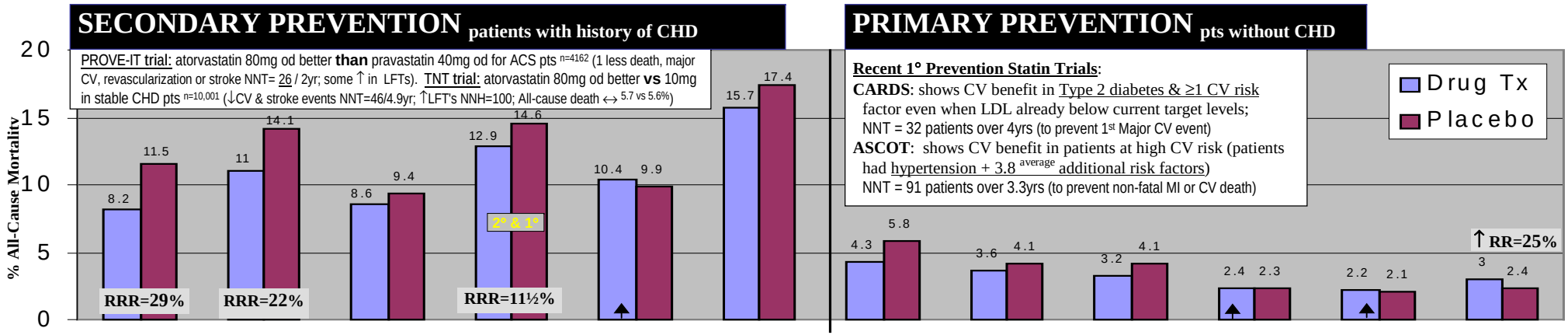
Figure 3. ALL-CAUSE MORTALITY OUTCOMES from MAJOR LIPID TRIALS



	4S	LIPID	CARE	HPS	BIP	VA-HIT	CARDS	ASCOT	WOSCOPS	AFCAPS	HHS	WHO-CLOF
Drug & dose used	**Simvastatin** 20-40mg/day[1,2]	**Pravastatin** 40mg/day [3,4]	**Pravastatin** 40mg/day [5]	**Simvastatin** 40mg/d [6,7,8,9,10]	**Bezafibrate** 400mg/day [11]	**Gemfibrozil** 600mg BID [12]	**Atorvastatin** 10mg/day[13]	**Atorvastatin** 10mg/day [14]	**Pravastatin** 40mg/day [15]	**Lovastatin** 20-40mg/day [16]	**Gemfibrozil** 600mg BID [17]	**Clofibrate** 1.6g/day [18]
ARR all death	**3.3%** p=0.0003	**3.1%** p<0.001	**NS**	**1.7%** p<0.001	**NS**	**NS**	**NS**	**NS**	**0.9% p=0.051**	**NS**	**NS**	**(-0.6%)** p <0.05
NNT	30	32	**NS**	**57**	**NS**	**NS**	**NS**	**NS**	**111 (p=0.051)**	**NS**	**NS**	**NNH=167**
Duration	5.4 yrs	6.1 yrs	5 yrs	5 yrs	6.2 yrs	5.1 yrs	4 yrs	3.3 yrs	4.9 yrs	5.2 yrs	5 yrs	5.3 yrs
All-cause mortality in *English* based on NNT	**Treat 30 patients for 5.4 yrs to prevent 1 death**	**Treat 32 patients for 6.1 yrs to prevent 1 death**	No statistical difference in all-cause mortality	**Treat 57 patients for 5 yrs to prevent 1 death**	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality; trial halted early	No statistical difference in all-cause mortality; trial halted early	**Trend: 1 death prevented per 111 patients over 4.9yrs**	No statistical difference in all-cause mortality	No statistical difference in all-cause mortality	Treating **167** patients for 5.3yrs **caused 1 extra death**
n= (♂+♀) ***publication yr***	3617+827 *1994*	7498+1516 *1998*	3583+576 *1996*	15454♂+5082♀ *2002*	2825♂ + 265♀ *2000*	2531♂ *1998*	1929 ♂ + 909 ♀ *Aug 2004*	8363♂+1942♀ *2003*	6595♂ *1995*	5608+997 *1998*	4081♂ *1987*	15745♂ *1978*
Patients studied	pts with angina or previous MI & TC >5.5 age 35-70	recent hx of acute MI or unstable angina; age 31-75	recent hx of acute MI & average LDL; age 21-75	High risk patients: MI, CHD, PVD, PVD, DM, HTN; TC ≥3.5; age 40-80	recent hx of MI or stable angina; age 45-74	♂ with CHD, low HDL & normal LDL; age <74	**Type 2 Diabetes** ≥1 risk factor; no CHD/CVD, LDL ≤4.14; age 40-75	**≥3** risk factors[CHD] **TC ≤6.5 & HTN** (24% diabetes) age 40-79	♂ with cholesterol **≥7**; (44% smokers) age 45-64	**↓HDL** but normal LDL& TC; ♂ 45-73yr & ♀ 55-73yrs	♂ with high levels of non-HDL cholesterol age 40-55	♂ with normal or high TC; age 30-59
LDL (ave) initial⇨end	**4.9⇨3.2**	3.9⇨2.9	3.6⇨2.5 †	3.3⇨2.3 (Adjusted ~ 3.9)[19]	3.9⇨3.6	2.9;↔LDL	3.0⇨2.1	3.4⇨2.3	5⇨4.1	3.9⇨3.0	4.9⇨4.5	not available
1° Endpoint Placebo/Drug	↓ total mortality 11.5%/8.2% NNT=31	↓ death CHD 8.3%/6.4% NNT=53	↓ MI / death CHD 13.2/10.2% NNT=34	↓Vascular fatal & non 25.2/19.8% NNT=19	MI or death sudden NS 15% / 13.6%	↓ MI / death CHD 21.7/17.3% NNT=23	↓1st CHD Event 9.0%/5.8% NNT=32	↓MI /death CHD 3%/1.9% NNT=91	↓MI /death CHD 7.9%/5.5% NNT=42	↓ 1st CV event 10.9/6.8% NNT=25	↓ MI / death CHD 41.4/27.3% NNT=8	↓ heart disease
Comment	impact after~1 yr 10yr data NNT=42		benefit most in ♀ & high LDL baseline	benefits similar in low & high LDL	benefit only in pts with *TG* >2.3	some benefit in ↑HDL & ↓TGs	benefit even in LDL ⇨ <2	benefit only in ♂; especially >60yrs	higher risk ♂ pts	Serious adverse outcome events 34% in both groups	↑ in non-CHD mortality?	↑ death; ↑ liver/GI risk
	STATINS				**FIBRATES**		**STATINS**				**FIBRATES**	

ACS=acute coronary syndrome ARR=% absolute risk reduction CHD=coronary heart disease CV=cardiovascular CVD= cardiovascular death DM=diabetes GI=gastrointestinal hx=history LFTs=liver function tests MI=myocardial infarction MI NF =nonfatal MI NNH= # needed to harm one NNT= # needed to treat to benefit one (e.g. in 4S trial, treating 30patients for 5.4yr would prevent 1 death) NS= not statistically significant pts=patients RRR= relative risk reduction Tx= treatment † in the CARE trial pts with initial LDL < 3.2 did not receive CV benefit from pravastatin; Lipid values in mmol/L (HDL= high density lipoprotein LDL= low density lipoprotein TC= total cholesterol TG= triglycerides)

NOTE: This collection of data is from different studies of varying patient groups and with varying methodology; it presents data and demonstrates overall trends but can not be used for direct quantitative comparison.

Summary of All-Cause Mortality Evidence

{ many studies not powered to evaluate this endpoint ; of published trials, only the 4S & HPS "overall" had this as the primary (1°) endpoint }

- **Statins** [20,21]: strong evidence for 2° prevention (including high-dose atorvastatin 80mg in ACS [22]); some evidence for 1° prevention in diabetes & male pts at ↑'d risk of CHD.
- **Fibrates**: **no** evidence yet for reductions in 1° or 2° all-cause mortality[23]; possible benefit in subset of patients with low HDL, TG's >2.3 &/or pts with diabetes
- **Lack data** to assess **risk vs benefit** in: 1) age ≥80 2) combination therapy 3) 1° prevention in low risk pts 4)aggressive pursuit of targets

Trials support *statins* for *high risk* rather than just *high TC or LDL*; few *treat to target* trials e.g.TNT.

TNT: CV benefit in 2° prevention with achieved LDL of 2.0 80mg atorv vs 2.6 10mg atorv mmol/L; however a non significant ↑ in non-CV death 3.2 vs 2.5% & ↑LFTs 1.2 vs 0.2%

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